DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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March 25, 2002

Donald E. Wilson, M.D., M.A.C.P.
Dean, School of Medicine
University of Maryland, Baltimore
655 West Baltimore Street
Baltimore, Maryland 21201-1559

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1174

Research Project: Prospective, Randomized, Muti-Center Trial of 12 ml/kg vs. 6 ml/kg Tidal Volume Positive Pressure Ventilation for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome
Principal Investigator: Henry Silverman , M.D.
RPN Number: 429161-109502

Research Project: Prospective, Randomized, Muti-Center Trial of 12 ml/kg vs. 6 ml/kg Tidal Volume Positive Pressure Ventilation and Ketoconazole vs. Placebo for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome
Principal Investigator: Henry Silverman , M.D.
RPN Number: 429161-109502

Research Project: A Phase II/III, Randomized, Double-Blinded, Placebo-Controlled Trial of Lisofylline vs. Placebo in Patients with Acute Lung Injury and Acute Respiratory Distress Syndrome
Principal Investigator: Henry Silverman , M.D.
RPN Number: 1098113

Research Project: Prospective, Randomized, Muti-Center Trial of 12 ml/kg vs. 6 ml/kg

Tidal Volume Positive Pressure Ventilation and Lisofylline vs. Placebo for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome

Principal Investigator: Henry Silverman , M.D.

RPN Number: 0298116

Research Publication: Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome (N. Engl J Med 2000;342:1301-8)

HHS Project Number: N01-HR46063

Dear Dr. Wilson:

The Office for Human Research Protections (OHRP) has reviewed the University of Maryland at Baltimore's (UMB's) March 5, 2002 report that was submitted in response to OHRP's February 4, 2002 letter to UMB regarding the allegations of possible noncompliance with the Department of Health and Human Services (HHS) regulations for protection of human subjects (45 CFR Part 46) involving the above referenced research. OHRP acknowledges that the research has been completed.

Based upon its review, OHRP makes the following determinations regarding the above-referenced research:

(1) In its February 4, 2002 letter, OHRP found that the informed consent documents reviewed and approved by the UMB Institutional Review Board (IRB) failed to adequately describe the reasonably foreseeable risks and discomforts of the research, in accordance with the requirements of HHS regulations at 45 CFR 46.116(a)(2). In specific, OHRP found that the informed consent documents failed to describe the following risks and potential discomforts associated with the non-traditional, 6 ml/kg tidal volume group that were described in the UMB IRB-approved protocol: dyspnea, agitation, potential need for higher doses of sedatives and paralytics, volume overload, and hypernatremia.

Corrective Action: OHRP acknowledges that the current UMB IRB procedures would require that all the risks and potential discomforts that the subject would be expected to undergo are described in the informed consent document. OHRP finds this corrective action to be satisfactory and appropriate under the UMB MPA.

(2) HHS regulations at 45 CFR 46.117(a) require that informed consent be documented by use of a *written* consent form approved by the IRB and that is signed by the subject or the subject's legally authorized representative, unless the IRB waives this requirement in accordance with 45

CFR 46.117(c). In its February 4, 2002 letter, OHRP found that the UMB IRB-approved informed consent documents permitting witnessed telephone consent by the subject's legally authorized representative fail to comply (i) with the requirements for waiver of documentation of informed consent as required by 45 CFR 46.117(c); and (ii) with the provisions for informed consent described in the protocol.

Corrective Action: OHRP acknowledges that the current UMB IRB procedures would not permit witnessed telephone consent by a subject's legally authorized representative. OHRP finds this corrective action to be satisfactory and appropriate under the UMB MPA.

(3) OHRP finds that UMB has adequately addressed the additional concerns raised by OHRP in its February 4, 2002 letter.

As a result of the above determinations, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Anne N. Hirshfield, Assistant Dean for Research, UMB
Dr. Paul Fishman, Chair, IRB Chair, UMB
Dr. John Mather, Director, Office of Research Compliance and Assurance, Veterans Health

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